

# UNIVERSITY OF CAMBRIDGE : DEPARTMENT OF GENETICS

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Our Ref:GAD/JH

8th November, 1982.

Dr. Maxine Singer,  
Department of Health, Education & Welfare,  
National Institute of Health,  
Building 37, Rm 4E28,  
Bethesda,  
Maryland 20205,  
U.S.A.

Dear Maxine,

No doubt you've seen Lewin's report on molecular drive (Science 218 552-3). At least he's got right that molecular drive is a system of (a) fixation and (b) with a particularly synchronous pattern of fixation. However, there are a few remarks by commentators which puzzle me, at least those of Jeffreys. We've replied to these and I'm enclosing a copy of our letter to Science. With respect to Alu, I guess he's picked up on your remarks at Heidelberg i.e. the absence of a difference in within- and between-species divergence in the primate Alu. Where are these data published? I'm very interested to look at them. I'm not sure if they were your own data. If they are, could you send me a copy of any paper you have on this, if it's not yet published?

You'll see from our enclosed letter, that we regard the observed levels of divergence at any one time to reflect the differences in rates between homogenisation and mutation. There are many factors influencing this, not least the family itself. What really interests us is if there has ever been a systematic search for a species diagnostic variant, indicative of separate homogenisation in each primate species? Unless this is done, in the way for example Steve Brown did in the MIF-family, then it's always difficult to interpret divergence levels. This is especially difficult if the levels are taken from a handful of clones in each species. A family like Alu with 500,000 members is bound to have both divergent isolated members and also a subfamily structure. The question is what do the clones really represent? We know that MIF in 5 species of rodents has several subfamilies (i.e. partial homogenisation of a diagnostic variant); however surprisingly these subfamilies are present in all species - but to different extents (data in preparation). There are several complex interpretations of these patterns, but nevertheless the differences in abundance of the different subfamilies between species, suggests that MIF is undergoing a process of homogenisation in each species and that different subfamilies are either on the way in or on the way out. Or alternatively the constraints on large family total homogenisation might lead to an equilibrium situation.

All these types<sup>of</sup> data come from whole-family analysis. They would not have been revealed by sequencing a few clones - although we have this as well in MIF which tell us other things as well - but that's another story. So even though there has been a clear homogenisation between rodent and human Alu family counterparts (see enclosed) - revealed mainly by whole family studies - the question is, is it really

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as slow as to be only detectable when one goes as far back in the species phylogeny as rodent versus man. Could it be that there are also distinct whole family or subfamily differences between primate species indicative of a faster rate of homogenisation?

Is there anything in the Alu data that throws any light on this? Or better, are there any data that definitely rules out some homogenisation since primate species separation? Given the debate now initiated in Science, we are very eager to know.

With very best regards.

Yours sincerely,

G. A. Dover. 

Enc.